Remarks / Arguments

I.

Support for Amendments

Changes made to an application that are supported by information disclosed in the specification are not generally considered new matter. That is, the claims may recite functional elements occurring in response to structures or configurations as already claimed. For instance, *In re Smythe*, 178 USPQ 279, 285 (C.C.P.A. 1973) stated the general rule for determining when the subject matter is inherently disclosed in the specification:

> "By disclosing in a patent application a device that inherently performs a function, operates according to a theory, or has an advantage, a patent application necessarily discloses that function, theory or advantage even though he says nothing concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibitory new matter."

Thus, clarification as to theory or function of the invention can be set forth in view of the inherent disclosure of the application. *In re Nathan*, 140 USPQ 601 (C.C.P.A. 1964) further confirmed this when stating, "[S]ubsequent clarification of or a change in an original disclosure does not necessarily make that original disclosure fatally defective." Further, information that is an inherent property of material adequately disclosed in the specification of the application can be claimed. *Ex parte Davisson*, 133 USPQ 400 (Pat. Off. Bd. Ap. 1958).

Turning to the amendments, claim 1 is amended to provide that recombination occurs between said different constructs at said first recombination sequences and at said second recombination sequences after transformation. Similarly, claim 19 is amended to provide that said first and said second recombination sequences permit recombination *in vivo* between said different constructs at said first recombination sequences and at said second recombination sequences. As will be explained, the recombination events are inherent functions of the methods and compositions as claimed and as discussed throughout the application.

For instance, page 5, ll. 15-19 provides that in the transformed moss cells recombination events occur between two constructs having similar recombination sequences that are positioned at different sites,

> "Thus the two constructs comprise similar complementary recombination sequences located at different sites therein that enable or permit the constructs to recombine with each other in situ in transformed moss protonema cells comprised in the moss protonema, for example protonema of Physcomitrella patens."

Page 6, ll. 11-17 also confirms that recombination events occur between the two constructs at the recombination sequences,

> "Naturally, the skilled addressee will appreciate that the heterologous constructs of the invention will comprise recombination sequences in appropriate position and orientation that enables recombination events to occur between the two. The recombination nucleotide sequences of constructs of the invention can be of any length provided that they are capable of causing or permitting recombination events to occur."

Thus recombination is demonstrated to occur between the constructs at the first recombination sequences and at the second recombination sequences. Turning now to the Examples section, specific construct configurations and sequences are demonstrated for recombination events. For instance, SEQ ID NO 3 is provided as a first recombination sequence, which is oriented at the 5' end for a first construct (*see* page 18) and at the 3' end for a second construct (*see* page 20). SEQ ID NO 6 is provided as a second recombination sequence, which is oriented at the 3' end for the first construct (*see* page 19) and at the 5' end of the second construct (*see* pages 19-20). Thus, the first construct is shown to have the first recombination sequence at the 5' end and the second recombination sequence at the 3' end. The second construct is shown to have the second recombination sequence at the 5' end and the first recombination sequence at the 3' end.

Thus, the application confirms structurally that the two different constructs incorporate

the same recombination sequences, yet they differ in position. For completeness, these limitations are set forth in the claims. Once the moss cell is transformed with the constructs, the recombination event can occur between constructs at the first recombination sequences and at the second recombination sequences.

Further, increased copy number of an inserted heterologous sequence was demonstrated in a stably transformed plant at page 24. As such, clams 1 and 19 are supported by the specification.

Claim 27 is amended to provide that the heterologous sequences obtained from the recombination are integrated into the moss plant cell's genome. Similarly, claim 28 is amended to provide that the first and second recombination sequences permit integration of heterologous sequences obtained from the recombination into the moss plant cell's genome. Support for these amendments can be found above with respect to the amendment of claim 1, which confirms integration of heterologous sequences from recombination events into a moss plant cell's genome. Further support may be found at page 15, ll. 1-6,

> "As discussed above, the present inventors show that enhanced expression from constructs of the invention introduced (preferably at high levels) into the protoplasts of a moss, preferably at high cell density, such as Physcomitrella patens, which constructs are integrated into the genome give rise to transcribed mRNA."

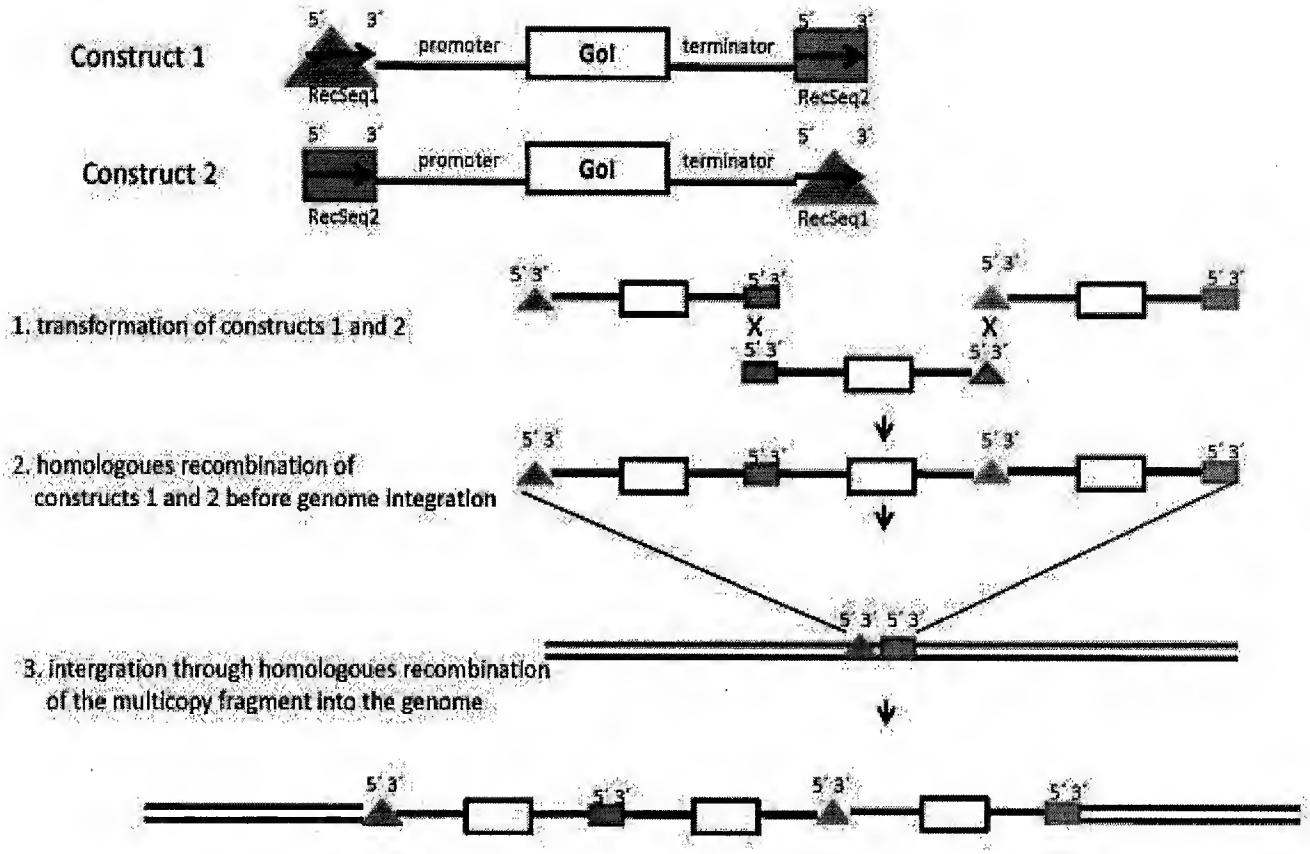
II.

Introduction to the Invention

As a review, the present invention provides methods and systems for amplifying gene expression in a transformed moss plant cell. Broadly, the invention includes at least two constructs, each having at least one heterologous nucleotide sequence. The first construct is flanked at the 5' end by a first recombination sequence and is flanked at the 3' end by a second recombination sequence. The second construct is flanked at the 5' end by the second recombination sequence and is flanked at the 3' end by the first recombination sequence. This configuration permits the constructs to recombine with each other. The inventors surprisingly

found such a system results in an increase in the integrated copy number of heterologous nucleic acid constructs in regenerated tissue which in turn correlated with increased protein expression levels.

A diagram overview of the general technical approach is summarized below. Referring to the below diagram, two constructs are created, each construct including a gene of interest operably linked to a promoter and a terminator sequence; each construct flanked by recombination sequences RecSeq1 and RecSeq2. More specifically, two variants of the operational gene are constructed. The first is flanked at the 5' end with recombination sequence 1 (RecSeq1) and flanked at the 3' end with recombination sequence 2 (RecSeq2). The second is flanked at the 5' end with recombination sequence 2 (RecSeq2) and flanked at the 3' end with recombination sequence 1 (ReqSeq1). The moss cell is transformed with both constructs and homologous recombination occurs between the constructs to form a multicopy product. After this first recombination step, the multicopy product is integrated into the moss cell genome, in this case preferably via homologous recombination.



III.

Response to Claim Rejections Under 35 U.S.C. § 112

A. Claims 1 and 19 comply with 35 U.S.C. § 112, second paragraph

Claims 1 and 19 are rejected under 35 U.S.C. § 112, first paragraph, as lacking support for the recited element, "wherein said first and said second recombination sequences form a set of recombination sequences designed to enable said at least first and said at least second constructs to recombine with each other in vivo." Specifically, the Examiner contends Applicant does not demonstrate possession of the claimed invention.

This element is supported throughout the application as indicated in the Response to Office Action filed April 15, 2010, such as at pages 3, 18, 19 and in particular page 4, ll.19-22, which provides, "The at least first and the at least second recombination sequences form a set

that make it possible for the constructs of the invention to recombine with each other."

To expedite allowance of the application this passage has been amended in claim 1 to provide, "recombination occurs between said different constructs at said first recombination sequences and at said second recombination sequences after transformation." Support for this amendment is demonstrated above in Section 1 of this Response. Accordingly, Applicant respectfully requests the rejections be withdrawn and the claims allowed.

B. Claim 20 complies with 35 U.S.C. § 112, first paragraph

Claim 20 is rejected under 35 U.S.C. § 112, first paragraph, as not supporting the element, "wherein the mammalian cell is an established cell line or primary culture." This element is not recited in claim 20. Claim 20 refers to a set of nucleic acid vectors that provide linear DNA constructs. For completeness, the invention utilizes moss as recited in independent claims 1 and 19. Applicant respectfully requests the rejection be withdrawn and the claim allowed.

C. Claims 27 and 28 comply with 35 U.S.C. 112, second paragraph

Claims 27 and 28 are rejected uner 35 U.S.C. § 112, second paragraph as being indefinite. Specificially, the Examiner is confused as to the meaning of "said set of recombination sequences enable integration of heterologous sequences obtained from recombined at least first and at least second constructs into the moss plant." To clarify the invention, the below amendments are provided.

Claim 27 is amended to recite that heterologous sequences obtained from said recombination are integrated into the moss plant cell's genome. Since this element clearly defines the meets and bounds of the invention the claim is definite as amended.

Claim 28 is amended to recite that said first and second recombination sequences permit integration of heterologous sequences obtained from said recombination into the moss plant cell's genome. Since this element clearly defines the meets and bounds of the invention the claim is definite as amended.

Applicant respectfully requests the rejections be withdrawn and the claims allowed.

IV.
Conclusion

In view of the above remarks, Applicant respectfully requests all rejections be withdrawn and a notice of allowance be issued. The Examiner is invited to contact the attorney of record below should there be further questions regarding the application.

Respectfully submitted,

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